IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Before the Board of Patent Appeals and Interferences

In re the Application of

Inventor	**:**	**Matthew Bruce et al.**
Application No.	**:**	**10/597,532**
Filed	**:**	**July 28, 2006**
For	**:**	**ULTRASONIC IMAGING OF PERFUSION AND BLOOD FLOW WITH HARMONIC CONTRAST AGENTS**

APPEAL BRIEF

On Appeal from Group Art Unit 3768
Examiner Hien Ngoc Nguyen

W. Brinton Yorks, Jr.

US PHILIPS CORPORATION
22100 Bothell Everett Highway
Bothell, WA 98021
Phone: (425) 487-7152
Fax: (425) 487-8135
email: brint.yorks@philips.com

Attorney for Appellants

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I. REAL PARTY IN INTEREST

The real party in interest is Koninklijke Philips Electronics N.V., Eindhoven, The Netherlands by virtue of an assignment recorded July 28, 2006 at reel 018018, frame 0027.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF CLAIMS

This application was originally filed with Claims 1-20. In response to a restriction requirement, Claims 1-10 were elected and Claims 11-20 were amended to depend from elected Claims 1-10. Claims 1-10 stand finally rejected and Claims 11-20 were incorrectly characterized as withdrawn by an Office Action mailed January 25, 2010. Claims 1-20 are the subject of this appeal.

IV. STATUS OF AMENDMENTS

No amendments or other filings were submitted in response to the final rejection mailed January 25, 2010. A notice of appeal was timely filed on April 13, 2010.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

Ultrasonic imaging of blood vessels can be enhanced by the use of injected microbubble contrast agents into the blood stream of the patient. The microbubbles return echo signals at a harmonic of the transmitted frequency, enabling them to be clearly distinguished in the image. Thus, contrast agents are effective when the vasculature of a patient is being diagnosed. However, the progression of infusion of the contrast agents into the microvasculature of tissue will soon surround larger vessels with tissue perfused with contrast agents, diminishing the distinction of the contrast agent in larger vessels being examiner from the contrast agent in the surrounding microvasculature. The larger blood vessels will thus soon blend into the background tissue. The present invention addresses this problem by processing echo signals in two different ways. The different processing reveals and distinguishes the signals from blood vessels differently from those from tissue perfusion. The differently processed signals are utilized to produce the portion of the image depicting perfusion and the portion of the image depicting the blood flow in larger vessels. The two are combined to display blood flow in larger vessels clearly distinguished from the surrounding tissue perfusion with blood.

Claim 1 is supported by the drawings and specification as seen by reference numerals (#) of the drawings and the specification text (pg., ln) as follows:

1. A method of ultrasonically imaging blood perfusion and blood flow in a region of interest of a body comprising:
acquiring a sequence of ultrasonic echo signals from a body which has been infused with an ultrasonic contrast agent {#12,#18; pg. 4, ln 31-pg. 5, ln 14};
processing the echo signals to detect the tissue structure in the absence of microbubbles {#22, pg. 5, ln 26-28};
processing a plurality of the echo signals in a first way to detect echo signals returned from tissue microvasculature perfused with the contrast agent {#24, pg. 5, ln 26-29};
processing a plurality of the echo signals in a second way to detect echoes returned from blood flow containing the contrast agent in larger vessels {#30, pg. 6, ln 6-18};
utilizing the echo signals processed the first way to form a portion of an image depicting perfusion {#32; pg 6, ln 16-25};
utilizing the echo signals processed the second way to form a portion of an image depicting blood flow in larger vessels {#32; pg 6, ln 16-25}; and
displaying an ultrasound image depicting both contrast-enhanced perfusion and contrast-enhanced blood flow {#38; pg 6, ln 25-26} .

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether Claims 1-7 and 9 were correctly rejected under 35 U.S.C. §102(b) as being anticipated by US Pat. Appl. Pub. No. 2003/0204142 (Brock-Fisher et al.)

B. Whether Claim 8 was correctly rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of US Pat. 6,095,980 (Burns et al.)

C. Whether Claim 10 was correctly rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of Burns et al. and further in view of US Pat. 6,620,103 (Bruce et al.)

VII. ARGUMENT

A. Whether Claims 1-7 and 9 were correctly rejected under 35 U.S.C. §102(b) as being anticipated by US Pat. Appl. Pub. No. 2003/0204142 (Brock-Fisher et al.)

Claims 1-7 and 9 were rejected under 35 U.S.C. §102(b) as being anticipated by US patent publication US2003/0204142 (Brock-Fisher et al.) which is assigned to the same assignee as the present invention. Claim 1 describes a method of ultrasonically imaging blood perfusion and blood flow in a region of interest of a body comprising acquiring a sequence of ultrasonic echo signals from a body which has been infused with an ultrasonic contrast agent; processing the echo signals to detect the tissue structure in the absence of microbubbles; processing a plurality of the echo signals in a first way to detect echo signals returned from tissue microvasculature perfused with the contrast agent; processing a plurality of the echo signals in a second way to detect

echoes returned from blood flow containing the contrast agent in larger vessels; utilizing the echo signals processed the first way to form a portion of an image depicting perfusion; utilizing the echo signals processed the second way to form a portion of an image depicting blood flow in larger vessels; and displaying an ultrasound image depicting both contrast-enhanced perfusion and contrast-enhanced blood flow. When a clinician is imaging with contrast agents, he is generally trying to use the contrast agent to image blood flow in large blood vessels, or to assess the perfusion of the microvasculature in tissue. However since blood vessels and tissue are intermingled in the body and thus usually intermingled in the ultrasound image, it is often difficult to discern whether contrast agent is in one or the other. The present invention enables the flow in blood vessels and tissue microvasculature to be distinguished or segmented by processing echo signals from contrast in two different ways, one which preferentially detects echo signals from the contrast agent in tissue microvasculature and another which preferentially detects echo signals from blood flow in larger vessels. The two types of blood flow can then be distinguished in their respective locations in the image as by highlighting or shading or coloring them differently so that the clinician encounters no ambiguity which trying to diagnose either tissue perfusion characteristics or vessel blood flow characteristics.

Brock-Fisher et al. are not concerned with and do not suggest how to distinguish tissue perfusion from larger vessel blood flow. They are concerned with reducing echoes from tissue and stationary contrast agent so that the color flow image will only highlight flowing contrast agent. This is done with two clutter filters, one which removes tissue echo signals and a second which removes echo signals from stationary contrast agent microbubbles. The common characteristic of tissue and stationary microbubbles is that their velocity of movement measured by the Doppler shift is at or near zero: tissue generally moves much slower than blood flow, if at all, and stationary microbubbles likewise have a velocity at or near zero. The sequence of removing these signals is shown in Fig. 9 of Brock-Fisher et al. In step 910 the responses from tissue are suppressed from the echoes. As explained in paragraph [0083], the tissue response is removed by a clutter filter in a tissue-signal processor 810. The echo signals with the tissue response removed are then processed by a color flow algorithm in step 912. As stated in paragraph [0087], the color flow algorithm includes another clutter filter 500 which removes the effect of echoes from stationary microbubbles. What is left is echo signals from blood flow, which is imaged. As Brock-Fisher et al. state in paragraph [0077], "the cumulative effect of the two filters and the power-modulation technique(s) is to reduce tissue generation signals and

stationary contrast-bubble signals, while passing signals generated from moving contrast-agent bubbles." This is a very good way to image the blood flow in larger vessels where the contrast agent flows freely, as other motional effects have been eliminated.

Fig. 10 of Brock-Fisher et al. adds a further improvement, which is to correct blood flow velocity measurements for the motion of tissue in which the blood flow occurs. The ultrasound probe, being stationary on or in the body, will measure all velocities as relative to the speed of the probe, which is zero. But suppose a blood vessel had a blood flow velocity of 4 cm/sec and the vessel was in moving tissue such as a coronary artery on the myocardium of the heart. Since the myocardium is always moving as the heart beats, components of this tissue motion will add or subtract from that of the coronary blood flow. If the heart is moving in the same direction as the blood flow, the combination of the two will be seen by the probe; a 2 cm/sec component of motion in the same direction as the 4 cm/sec blood flow will appear to have a velocity of 6 cm/sec to the stationary probe. The embodiment of Brock-Fisher et al.'s Fig. 10 compensates for this.

Both of these embodiments are seen to be unconcerned with perfusion, and in particular to segmenting tissue perfusion from larger vessel blood flow by different ways of processing. In fact, the word

"perfusion" is only mentioned twice in the application, once in paragraph [0005] where it is stated that contrast agents are effective for detecting perfusion and again in paragraph [0027] where it is said that the Brock-Fisher et al. invention can be used for blood-perfusion imaging. But Brock-Fisher et al. are silent on any way to segment microvasculature perfusion from larger vessel blood flow. In Claim 1, the steps of processing in the first and second ways and the following two utilizing steps are seen to be neither shown nor suggested by Brock-Fisher et al. On page 8 of the Final Rejection, the Examiner seems to want the specific parameters used in a described embodiment of the present application, velocity variance and echo signal power, to be recited in the claim. But since the limitations already recited in the claim are not found in Brock-Fisher et al., there is no need to recite details of a described embodiment to make the claim patentable. The claim elements as presently described are simply not found in Brock-Fisher et al. Thus it is respectfully submitted that Brock-Fisher et al. cannot anticipate Claim 1 or its dependent Claims 2-20.

Claims 11-20 are seen to depend from Claim 1. It is therefore respectfully submitted that Claims 11-20 are not anticipated by Brock-Fisher et al. and are patentable by reason of their dependency.

B. Whether Claim 8 was correctly rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of US Pat. 6,095,980 (Burns et al.)

Claim 8 was rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of US Pat. 6,095,980 (Burns et al.) Burns et al. was cited for its reference to the pulse inversion technique for nonlinear (harmonic) separation, although pulse inversion was also mentioned in Brock-Fisher et al. in paragraph [0065]. It is seen that Burns et al. are concerned with segmenting signals from tissue motion, harmonic contrast agents, and harmonic signals from tissue. Like Brock-Fisher et al., Burns et al. are unconcerned with segmenting microvasculature perfusion from larger vessel blood flow. The term perfusion is mentioned only once by Burns et al., to say that power Doppler is a good technique for imaging perfused tissue. Like Brock-Fisher et al., the steps of processing in the first and second ways and the following two utilizing steps of Claim 1 are seen to be neither shown nor suggested by Burns et al. Accordingly it is respectfully submitted that the combination of Brock-Fisher et al. and Burns et al. cannot render Claim 1 and its dependent claims including Claim 8 unpatentable.

C. Whether Claim 10 was correctly rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of Burns et al. and further in view of US Pat. 6,620,103 (Bruce et al.)

Claim 10 was rejected under 35 U.S.C. §103(a) as being unpatentable over Brock-Fisher et al. in view of Burns et al. and further in view of US Pat. 6,620,103 (Bruce et al.) Bruce et al. are detecting slow-moving microbubbles by time-interleaving the pulse pairs that are transmitted along each line of the image field. Since the microbubbles are moving very slowly, they only have to be interrogated at widely spaced intervals to detect their motion. A moving target indicator can then be used to detect their low velocity or their progressive locations marked on the ultrasound image in what is known as "bubble-tracking." Like the other two citations, Bruce et al. are unconcerned with segmenting contrast perfusion of tissue microvasculature from flowing contrast in larger vessels. The word perfusion is mentioned only once by Bruce et al., in the second paragraph of the patent. Like Brock-Fisher et al. and Burns et al., the steps of processing in the first and second ways and the following two utilizing steps of Claim 1 are seen to be neither shown nor suggested by Bruce et al. Accordingly it is respectfully submitted that the combination of Brock-Fisher et al., Burns et al., and Bruce et al. cannot render Claim 1 and its dependent claims including Claim 10 unpatentable.

It is further respectfully submitted that Claims 11-20, which depend from Claim 1, are patentable over Brock-Fisher et al., Burns et al., and Bruce et al. by reason of their dependency.

VIII. CONCLUSION

Based on the law and the facts, it is respectfully submitted that Claims 1-7, 9 and 11-20 are not anticipated by Brock-Fisher et al. and that Claims 8, 10 and 11-20 are patentable over any combination of Brock-Fisher et al., Burns et al., and Bruce et al. Accordingly, it is respectfully requested that this Honorable Board reverse the grounds of rejection of Claims 1-20 of this application which were stated in the January 25, 2010 Office action being appealed.

Respectfully submitted,

MATTHEW BRUCE ET AL.

By: /W. Brinton Yorks, Jr./
W. Brinton Yorks, Jr.
Reg. No. 28,923

June 12, 2010

APPENDIX A: CLAIMS APPENDIX

The following Claims 1-20 are the claims involved in this appeal.

1. (original) A method of ultrasonically imaging blood perfusion and blood flow in a region of interest of a body comprising:
acquiring a sequence of ultrasonic echo signals from a body which has been infused with an ultrasonic contrast agent;
processing the echo signals to detect the tissue structure in the absence of microbubbles;
processing a plurality of the echo signals in a first way to detect echo signals returned from tissue microvasculature perfused with the contrast agent;
processing a plurality of the echo signals in a second way to detect echoes returned from blood flow containing the contrast agent in larger vessels;
utilizing the echo signals processed the first way to form a portion of an image depicting perfusion;
utilizing the echo signals processed the second way to form a portion of an image depicting blood flow in larger vessels; and
displaying an ultrasound image depicting both contrast-enhanced perfusion and contrast-enhanced blood flow.

2. (original) The method of Claim 1, wherein displaying further comprises depicting both the presence and locations of microbubbles in tissue and the velocity of microbubbles in blood flow.

3. (original) The method of Claim 1, further comprising deciding the portion of the image which an echo signal is to form on the basis of a blood flow velocity estimation.

4. (original) The method of Claim 3, wherein deciding further comprises deciding the portion of the image which an echo signal is to form on the basis of a blood flow variance estimation.

5. (original) The method of Claim 1, wherein processing a plurality of echo signals in first and second ways comprises processing the same ensemble of echo signals in first and second ways.

6. (original) The method of Claim 1, wherein acquiring a sequence of ultrasonic echo signals further comprises acquiring an ensemble of echoes over time from each of a plurality of different locations in the body.

7. (original) The method of Claim 1, wherein processing a plurality of the echo signals in a first way comprises detecting the amplitude or power of the echo signals; and

wherein processing a plurality of the echo signals in a second way comprises Doppler processing the plurality of the echo signals.

8. (original) The method of Claim 7, wherein processing a plurality of the echo signals in both the first way and the second way both include detecting nonlinear components of the echo signals by the pulse inversion technique.

9. (original) The method of Claim 1, wherein utilizing the echo signals processed the first way further comprises forming a perfusion image; and

wherein utilizing the echo signals processed the second way further comprises forming a flow image; and

wherein displaying an ultrasound image further comprises displaying the perfusion image overlaid with the flow image.

10. (original) The method of Claim 1, further comprising transmitting a plurality of differently modulated transmit pulses in each of a plurality of different beam directions;

wherein processing a plurality of the echo signals in both the first way and the second way both include detecting harmonic components of the echo signals by the pulse inversion technique.

11. (previously presented) An ultrasonic diagnostic imaging system for imaging both perfusion and flow in a body infused with a contrast agent in accordance with the method of Claim 1 comprising:

an ultrasonic transducer array operated to transmit a plurality of pulses in each of a plurality of different beam directions and to receive echoes in response to the pulses;

a beamformer coupled to the transducer array;

a first processor for processing a plurality of the echo signals in the first way which is coupled to the beamformer and responsive to pluralities of echo signals for detecting echoes returned from perfused tissue;

a second processor for processing a plurality of the echo signals in the second way which is coupled to the beamformer and responsive to ensembles of echo signals for detecting echoes returned from blood flow containing contrast in larger vessels;

a decision processor, coupled to the first and second processors, for identifying signals to be displayed on the basis of velocity;

an image memory for the utilizing steps which is responsive to the decision circuit which acts to utilize signals produced by the first and second processors to form a perfusion image portion and a flow image portion; and

a display for the displaying step which is coupled to the image memory which displays an ultrasound image which depicts both contrast perfused tissue and the flow in larger vessels in a common image.

12. (original) The ultrasonic diagnostic imaging system of Claim 11, wherein the second processor includes a first signal path which Doppler processes nonlinear echo ensembles and a second signal path which Doppler processes fundamental frequency echo ensembles,

wherein the display displays an image of nonlinear Doppler processed flow in the near field and fundamental frequency Doppler processed flow in the far field.

13. (original) The ultrasonic diagnostic imaging system of Claim 11, further comprising a transmitter, coupled to the transducer array, which acts to transmit a plurality of differently modulated beams in each of a plurality of different beam directions.

14. (original) The ultrasonic diagnostic imaging system of Claim 13, wherein each of the first and second processors process harmonic signals separated by the pulse inversion technique.

15. (original) The ultrasonic diagnostic imaging system of Claim 11, wherein the decision processor acts to identify signals to be displayed on the basis of velocity variance.

16. (original) The ultrasonic diagnostic imaging system of Claim 15, further comprising a velocity variance estimator responsive to echo signals processed by the first and second processors and coupled to the decision processor.

17. (original) The ultrasonic diagnostic imaging system of Claim 11, wherein the image memory comprises a first image buffer for storing a perfusion image and a second image buffer for storing a flow image.

18. (original) The ultrasonic diagnostic imaging system of Claim 11, further comprising a tissue signal processor which acts to detect echoes from tissue in the absence of microbubbles.

19. (original) The ultrasonic diagnostic imaging system of Claim 18, wherein the display acts to selectively display an image which is less than all of the combination of a tissue image component, a perfusion image component, and a flow image component.

20. (original) The ultrasonic diagnostic imaging system of Claim 19, further comprising means for adjusting the opacity of one of the image components to be semi-transparent, whereby obscured tissue or flow may be visualized through the semi-transparent image component.

APPENDIX B: EVIDENCE APPENDIX

None. No extrinsic evidence has been submitted in this case.

APPENDIX C: RELATED PROCEEDINGS APPENDIX

None. There are no related proceedings.